staining and real-time PCR were used to detect the expression of IFN-γ from the aorta of ApoE-/-mice.

RESULTS Our results show that the percentages of CD4+ IFN-γ+ from the spleens were decreased after treatment with different dose of Danlou Tablet groups compared to the model group, greatly decreased with high-dose DLT group(model group vs DLT-H group :13.80±2.00 vs 8.23±1.65, $p < 0.01$). Immunohistochemical staining and real-time PCR for aorta revealed that the IFN-γ was decreaed with Danlou Tablet dose-dependent(the fold changes of IFN-γ:model group vs DLT-L group: 2.96±0.87 vs 2.10±1.28, $P < 0.05$; model group vs DLT-M group: 2.96±0.87 vs1.68±0.40, $P < 0.01$; model group vs DLT-H group: 2.96±0.87 vs1.24±0.15, $P < 0.01$). The findings suggest that Danlou Tablet could markedly attenuates progression of atherosclerosis by decreasing the expression of IFN-γ and suppressing inflammation.

CONCLUSIONS Our findings demonstrate that Danlou Tablet could decrease the expression of IFN-γ or restain the artery-infiltrating T cells, especially the Th1 cells activated or suppressed inflammation and attenuated progression of atherosclerosis via weaken the Th1-IFN-γ pathway.

GW26-e2323

Regulation and mechanism of Guizhi Decoction on Diabetic Cardiac Autonomic Neuropathy

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OBJECTIVES To investigate the effects of Guizhi decoction (a long-used harmonic prescription in traditional Chinese medicine) on cardiac autonomic neuropathy (CAN) in streptozotocin (STZ)-induced diabetic rats. With the establishment of chemical sympathetic sprouting and sympathectomy rat models, we explored the protective mechanism of Guizhi decoction on the cardiac sympathetic remodeling.

METHODS

1) After induction of diabetic rats with STZ for four weeks, mecobalamin and Guizhi decoction were administered to the STZ rats for 4 weeks. Heart rate variability (HRV) were recorded, and contents of nerve growth factor (NGF), growth associated protein 43(GAP-43) and ciliary neurotrophic factor (CNTF) in myocardium as well as the density of tyrosine hydroxylase (TH) and choline acetyltransferase (ChAT) in the right atrium (RA) were respectively measured using ELISA and immunohistochemical staining.
2) Cardiac sympathetic sprouting rats were induced with 4-Methylcatechol (4-MC) for 30 days. Metoprolol and Guizhi decoctions were separately administered to the rats for 30 days. Meanwhile, we established chemical sympathectomy rats with 6-Hydroxydopamine (6-OHDA) for 3 days. Mecobalamin and Guizhi decoctions were separately administered to the rats for 10 days. Contents of GAP-43, TH and ChAT in the cardiac tissue were examined and distribution of TH-positive nerve fibers was observed. Besides, serum myocardial enzyme levels and changes of myocardial morphology were observed in 6-OHDA rats.

RESULTS

1) STZ rats demonstrated autonomic nerve dysfunction. Compared with the model groups, rats treated with Guizhi decoction had higher HRV parameters such as SDNN, RMSSD, LF, HF and TP, as well as decreased LF/HF ($P < 0.05$); the TH-positive nerve fiber decreased while the ChAT-positive expression increased ($P < 0.05$); contents of GAP-43 and CNTF increased while NGF decreased ($P < 0.05$). It suggested that Guizhi decoction improved vagal nerve dysfunction in STZ diabetic rats and mitigated the autonomic neuropathy.
2) 4-MC caused cardiac sympathetic sprouting. Compared with the model group, contents of TH and GAP-43 in cardiac tissue decreased while ChAT unchanged in Guizhi decoction group, indicating that Guizhi decoction can effectively suppress the 4-MC-induced sympathetic sprouting.
3) 6-OHDA caused chemical sympathectomy. Compared with the model group, contents of TH and GAP-43 in myocardium of Guizhi decoction group elevated and ChAT kept unchanged; the serum levels of myocardial enzymes, the cardiac histopathology and heart function were improved, suggesting that Guizhi decoction effectively alleviated sympathetic injury and myocardial injury related to sympathetic denervation.

CONCLUSIONS Guizhi decoction effectively alleviated diabetic CAN. Guizhi decoction demonstrated double-sided regulation on cardiac sympathetic sprouting and sympathetic denervation which may be one of the important mechanism of the improvement of Guizhi Decoctionon on diabetic cardiomyopathy.

GW26-e4511

Blockade of Histone Demethylase JMJD2A Stimulates Endothelial Repair in Denuded Aorta of diabetic Rat

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OBJECTIVES Endothelial dysfunction is a central hallmark of diabetes, delaying endothelial healing in diabetic patients following angioplasty. The epigenetic abnormalities are increasingly considered to be relevant to the pathogenesis of diabetic complications. We here investigated the therapeutic potential of histone demethylase JMJD2A and its substrate histone H3 lysine 9 trimethylation (H3K9me3) on re-endothelialization in a vascular injury model of diabetic rats.

METHODS JMJD2A inhibition was achieved either by chemical inhibitor 2,4-pyridinedicarboxylic acid (2,4-PDCA) or small interfering RNA (siRNA) both *in vitro* and *in vivo* studies. *In vitro,* we examined the proliferative, migratory and angiogenic capacities of human umbilical vein endothelial cells (HUVECs) in response to high glucose (HG). Flow cytometry was performed to detect the apoptosis and the expressions of apoptosis-associated genes were assessed by real-time PCR and western blot. Immunoprecipitation (ChIP) assay was conducted to examine the modification of H3K9me3 at related genes' promoters. *In vivo*, common carotid artery balloon injury was developed in high-fat diets (60% fat) and low-dose streptozotocin (35 mg/kg) induced diabetic rats. The reendothelialization was quantified withEvens blue staining and immunohistochemical staining.

RESULTS Both in HG-treated HUVECs and balloon-injured arteries of diabetic rats, the global expression of JMJD2A was increased whereas H3K9me3 was decreased. *In vitro,* JMJD2A inhibition either by 2,4-PDCA (0.5mM) or by siRNA (20nM) accelerated HUVECs proliferation, migration and tube formation in response to HG, accompanied by reduced expression of TNF-α and suppressed apoptosis (down-regulated caspase3, caspase9, Bax and upregulated Bcl-2). ChIP assay indicated that the potential mechanism was relevant to the increased H3K9me3 at the promoter of TNF-a and then the transcriptional silencing of TNF-α. Complementary in vitro studies showed that JMJD2A inhibition promoted reendothelialization in diabetic rats.

CONCLUSIONS JMJD2A inhibition promotes reendothelialization after arterial injury in diabetic rats via accelerated proliferation, migration and suppressed apoptosis of endothelial cells.

GW26-e5383

Pioglitazone Decreases Plaque Thrombosis by Attenuating Plaque Inflammation. An In Vivo Study Using 18F-FDG PET/CT

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OBJECTIVES Pioglitazone, a clinically used insulin sensitizer, has appeared to have an anti-atherosclerotic effect. The aims of this study is to determine whether pioglitazone can reduce the number of plaque thrombosis incidences and whether decreasing plaque inflammation is the mechanism by which pioglitazone reduces plaque thromboses in an atherosclerotic model.

METHODS 20 male New Zealand white rabbits were randomly divided into two groups: Atherosclerosis group (Group A, n=10) and middle-pioglitazone-treated group (Group P, n=10). Atherosclerosis was induced in all rabbits by intermittent high-cholesterol diet and endothelial denudation. From the ninth week, the rabbits in group P received pioglitazone (10 $mg \cdot kg^{-1} \cdot d^{-1}$) in addition to the diet, till the end of experiment. PET/CT scans were performed at 8 week and 18 week in all survival rabbits, to obtain FDG uptake parameters (mean standardized uptake value, SUVmean and maximal standardized uptake value, SUVmax). Concomitantly, serum samples were obtained for analysis of blood glucose (G), triglycerides (TG), total cholesterol (Ch), HDL, LDL, hs-CRP and matrix metalloproteinase-9 concentration (MMP-9). All survival rabbits underwent 2 pharmacological triggerings to induce plaque rupture at 18 week. After pharmacological triggering, all rabbits were euthanatized, aortic histopathological analysis were performed.

RESULTS 20 male New Zealand white rabbits were randomly divided into two groups: Atherosclerosis group (Group A, n=10) and